Citation:

Cook NR, Kumanyika SK, Cutler JA, Whelton PK; Trials of Hypertension Prevention Collaborative Research Group. Dose-response of sodium excretion and blood pressure change among overweight, nonhypertensive adults in a three-year dietary intervention study.*J Hum Hypertens*. 2005 Jan; 19(1): 47-54.

PubMed ID: 15343354

Study Design:

Randomized controlled trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the relationship between sodium intake and blood pressure change in a 18-month and 36-month period, using data from the Trials of Hypertension Prevention (TOHP) II sodium intervention.

Inclusion Criteria:

- Moderately overweight (110% to 165% of the Metropolitan Life Insurance Company standards, body mass index (BMI) of 26.1 to 37.4 for men and 24.4 to 37.4 for women)
- Otherwise healthy
- Age 30 to 54 years
- Average diastolic blood pressure (DBP) 83 to 89mmHg and average systolic blood pressure (SBP) <140mmHg over nine measurements in three visits
- Valid baseline urinary sodium (UNa) excretion.

Exclusion Criteria:

- Treated for hypertension (HTN)
- Had cardiovascular disease, diabetes, renal insufficiency or other serious illness
- Pregnant or planning to become pregnant
- Unwilling or unable to adhere to trial procedures.

Description of Study Protocol:

Recruitment

Methods not described.

Design

Randomized controlled trial (RCT) parallel design.

Blinding Used

Research staff were blinded.

Intervention

TOHP II subjects were assigned to receive one of the following:

- Counseling for weight loss only
- Counseling for sodium intake reduction to 80mmol per 24 hours
- Counseling for weight loss and sodium intake reduction to 80mmol per 24 hours
- Usual care with no study delivered intervention
- Counseling was given by research staff (mainly by dietitian), in form of initial in-person one-on-one meetings, 10 weekly group meetings, four monthly group meetings, telephone contacts and face-to-face contacts
- Sodium intervention and usual care groups were combined for analysis.

Statistical Analysis

- Change in blood pressure (BP) was first examined by quintile of both level of sodium excretion achieved at follow-up and change from baseline, adjusted for age, ethnicity, sex, baseline BP and sodium excretion
- Test for trend over quintiles was performed using an ordinal variable in linear regression, with an additional adjustment for change in weight
- Repeated measured models for change in BP at 18 and 36 months were fit with adjustment for age, sex, ethnicity, clinic and baseline BP and sodium excretion
- Trends across the five categories were computed using the expected order at each time point.

Data Collection Summary:

Timing of Measurements

Screening, baseline, 18-month visit, 36-month visit. 25% of subjects also had a six-month visit.

Dependent Variables

- Blood pressure
- Urinary excretion of sodium and potassium.

Independent Variables

Assigned to sodium intake reduction to 80mmol per 24 hours or usual care with no study delivered intervention.

Control Variables

- Age
- Ethnicity
- Sex
- Clinic

- Baseline BP and sodium excretion
- Change in weight.

Description of Actual Data Sample:

- *Initial N:* 1,157 men and women, assigned to sodium reduction intervention (N=581) or usual care (N=576)
- *Attrition (final N):* 880 sodium reduction intervention (N=437) or usual care (N=443)
- *Age:* Average 44.2 years in sodium reduction group, average 43.2 years in usual care group
- *Ethnicity:* 17% black (no difference between groups)
- *Other relevant demographics:* 67% male (no difference between groups)
- *Anthropometrics:* Average 94kg body weight (no difference between groups)
- *Location:* Multicenter of nine locations in US.

Summary of Results:

Key Findings

- At 36 months, there were significant differences between sodium reduction group and usual care group in change of UNa excretion (-50.9mmol per 24 hours vs. -13.2mmol per 24 hours, P<0.0001), urinary sodium/potassium ratio (-0.62 vs. 0.06, P<0.0001), SBP (-1.2mmHg vs. 0.5mmHg, P=0.003) and DBP (-3.3mmHg vs. -2.4mmHg, P=0.04)
- At 18 months, there was a significant trend of greater SBP and DBP decrease with lower quintiles of sodium excretion (P<0.001)
- At 36 months, there was a significant trend of greater SBP decrease with lower quintiles of sodium excretion (P=0.005), but not with DBP (P=0.67).

Change in Variables of Interest from Baseline at Six, 18, and 36 months of Follow-up, Stratified by Treatment Assignment

Variable	Difference Between Groups	P-value
Urinary sodium excretion (mmol per 24 hours)		
Baseline	-1.9	0.69
Six-month change	-48.3	<0.0001
18-month change	-43.8	<0.0001
36-month change	-37.8	<0.0001
Urinary sodium/potassium ratio		
Baseline	-0.06	0.48
Six-month change	-0.88	<0.0001
18-month change	-0.66	<0.0001
36-month change	-0.68	<0.0001
Systolic blood pressure (mmHg)		
Baseline	0.6	0.15
Six-month change	-4.5	<0.0001

18-month change	-2.0	<0.0001
36-month change	-1.7	0.003
Diastolic blood pressure (mmHg)		
Baseline	0.2	0.04
Six-month change	-2.1	0.01
18-month change	-1.4	0.001
36-month change	-0.9	0.04

Author Conclusion:

- As reported previously, the TOHP II sodium reduction intervention was associated with an overall significant BP reduction over a three- to four-year period in this large sample of overweight men and women, leading to a significant decrease in the incidence of HTN. These detailed dose-response analyses in the data pooled for all participants help to quantify the extent of BP changes that can be expected to result from different degrees of sodium reduction
- There was generally a gradient of BP decreases according to category of attained sodium excretion, with larger BP decreases corresponding to a lower level of sodium achieved, and also in association with the degree of success in achieving and maintaining reduced sodium excretion levels.

Reviewer Comments:

Recruitment method was not described, published in previous articles.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes